

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

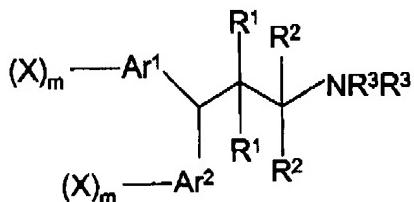
**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

Atty. Dkt. No. 072827-1905

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently amended) A method of treating a patient for depression comprising the step of ~~administering to said patient an effective amount of selecting a compound having a NMDA IC<sub>50</sub> of about 50 nM to about 1 μM as measured in the NMDA assay and a serotonin reuptake IC<sub>50</sub> of less than or equal to about 100 nm as measured in the serotonin reuptake inhibition assay; and~~  
administering to said patient an effective amount of said compound.
2. (Original) The method of claim 1, wherein said compound has an NMDA receptor IC<sub>50</sub> of 50 nM to 1 μM and a SSRI IC<sub>50</sub> less than 100 nM.
3. (Currently amended) A method of treating a patient for depression comprising the step of ~~administering to said patient an effective amount of selecting a compound having a NMDA IC<sub>50</sub> of about 50 nM to about 1 μM as measured in the NMDA assay and a serotonin reuptake IC<sub>50</sub> of less than or equal to about 100 nm as measured in the serotonin reuptake inhibition assay, wherein said compound has~~ having the chemical structure:



wherein each X is independently selected from the group consisting of -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, --OCF<sub>3</sub>, -O-alkyl, and -O-acyl;

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently selected from the group consisting of phenyl, naphthyl, thiofuranyl, tetrahydronaphthyl, furanyl, tetrahydrofuranyl, pyridyl, quinolinyl,

Atty. Dkt. No. 072827-1905

isoquinolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, cyclohexyl, cycloheptyl, and cyclopentyl;

each R<sup>1</sup> is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl;

each R<sup>2</sup> is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R<sup>2</sup>'s together are imino;

each R<sup>3</sup> is independently selected from the group consisting of -H, alkyl, 2-hydroxyethyl, and alkylphenyl; and

each m is independently an integer from 0 to 5;

provided that if both R<sub>3</sub>'s are -CH<sub>3</sub>, then both X<sub>m</sub>'s are not 3-F, 4-F, 3-CF<sub>3</sub>, 4-Cl, and if both R<sub>3</sub>'s are -CH<sub>3</sub> and one X<sub>m</sub> is 4-F then the other X<sub>m</sub> is not 4-Cl; further provided that if one R<sub>3</sub> is -H and the other R<sub>3</sub> is -CH<sub>3</sub> then both X<sub>m</sub>'s are not 4-Cl, and if one R<sub>3</sub> is -H and the other R<sub>3</sub> is -CH<sub>3</sub> then at least one m is 1;

or a pharmaceutically acceptable salt thereof.

4. (Previously presented) The method of claim 3 wherein for said compound each X is independently either -F, -Cl, -OCF<sub>3</sub> or -CF<sub>3</sub>;

each R<sup>1</sup> is -H;

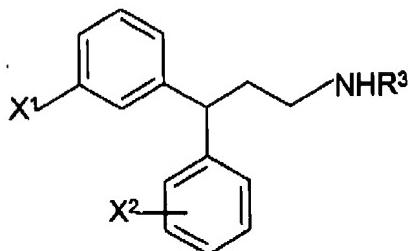
each R<sup>2</sup> is -H;

one R<sup>3</sup> is -H, and the other R<sup>3</sup> is either -H or -CH<sub>3</sub>; and

each m is 1.

5. (Currently amended) A method of treating a patient for depression comprising administering to said patient an effective amount of a compound having the chemical structure  
The method of claim 3 wherein said compound has the chemical structure:

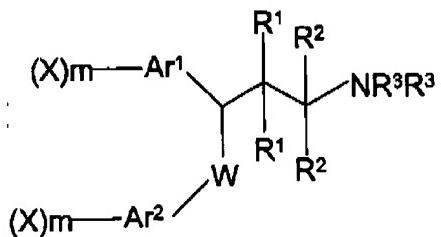
Atty. Dkt. No. 072827-1905



wherein  $X^1$  is either -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, -OCF<sub>3</sub>, -O-alkyl, or -O-acyl;  
 $X^2$  is either -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, -OCF<sub>3</sub>, -O-alkyl, or -O-acyl; and  
 $R^3$  is either -H or -CH<sub>3</sub>;  
or a pharmaceutically acceptable salt thereof.

6. (Original) The method of claim 5, wherein  $X^1$  is -F, -Cl, -OCF<sub>3</sub> or -CF<sub>3</sub>; and  $X^2$  is either 2-OCH<sub>3</sub>, 2-CH<sub>3</sub>, 3-F, 3-CF<sub>3</sub>, or 4-CF<sub>3</sub>.

7. (Withdrawn) A method of treating a patient for depression comprising the step of administering to said patient an effective amount of a compound having the chemical structure:



wherein each X is independently selected from the group consisting of -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, -OCF<sub>3</sub>, -O-alkyl, and -O-acyl;

W is selected from the group consisting of -CH<sub>2</sub>, -O-, and -S-;

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently selected from the group consisting of phenyl, naphthyl, thiofuranyl, tetrahydronaphthyl, furanyl, tetrahydrofuranyl, pyridyl, quinolinyl,

Atty. Dkt. No. 072827-1905

isoquinolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl cyclohexyl, cycloheptyl, and cyclopentyl;

each R<sup>1</sup> is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl;

each R<sup>2</sup> is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R<sup>2</sup>s together are imino;

each R<sup>3</sup> is independently selected from the group consisting of -H, alkyl, 2-hydroxyethyl, and alkylphenyl; and

m is 0 to 5;

or a pharmaceutically acceptable salt thereof.

8. (Withdrawn) The method of claim 7, wherein for said compound each X is independently either -F, -Cl, -OCF<sub>3</sub> or -CF<sub>3</sub>;

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently phenyl or naphthyl;

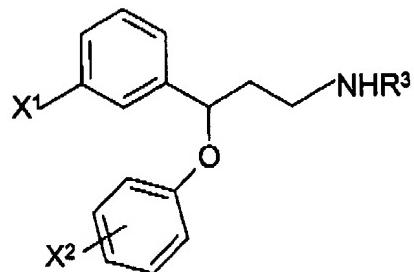
each R<sup>1</sup> is -H;

each R<sup>2</sup> is -H;

one R<sup>3</sup> is -H, and the other R<sup>3</sup> is either -H or -CH;

each m is 0 or 1.

9. (Withdrawn) The method of claim 7, wherein said compound has the chemical structure:



wherein X<sup>1</sup> is either -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, -OCF<sub>3</sub>, -O-alkyl, or -O-acyl;

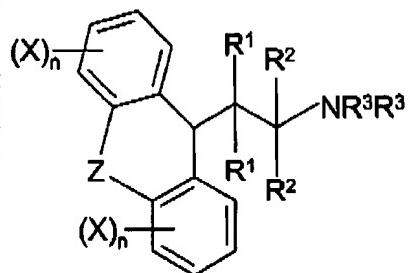
Atty. Dkt. No. 072827-1905

X<sup>2</sup> is either -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, —OCF<sub>3</sub>, -O-alkyl, or -O-acyl; and

R<sup>3</sup> is either -H or -CH<sub>3</sub>; or a pharmaceutically acceptable salt thereof.

10. (Withdrawn) The method of claim 9 wherein X<sup>1</sup> is either -F, -Cl, -OCF<sub>3</sub> or -CF<sub>3</sub>; and X<sup>2</sup> is either 2-OCH<sub>3</sub>, 2-CH<sub>3</sub>, 3-F, 3-CF<sub>3</sub>, or 4-CF<sub>3</sub>.

11. (Withdrawn) A method of treating a patient for depression comprising the step of administering to said patient an effective amount of a compound having the chemical structure:



wherein each X is independently selected from the group consisting of -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, —OCF<sub>3</sub>,

-O-alkyl, and -O-acyl;

each R<sup>1</sup> is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl;

each R<sup>2</sup> is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R<sup>2</sup>'s together are imino;

each R<sup>3</sup> is independently selected from the group consisting of -H, alkyl, 2-hydroxyethyl, and alkylphenyl;

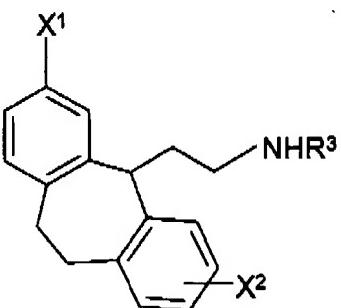
Z is either -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH(CH<sub>3</sub>)-, -CH=CH-, -O-CH<sub>2</sub>-, -S-CH<sub>2</sub>-, -CH<sub>2</sub>-, -O-, or -S-; and

Atty. Dkt. No. 072827-1905

each n is independently 1 to 4; or a pharmaceutically acceptable salt thereof.

12. (Withdrawn) The compound of claim 11, wherein each X is independently either -F, -Cl, -OCF<sub>3</sub> or -CF<sub>3</sub>;  
each R<sup>1</sup> is -H;  
each R<sup>2</sup> is -H;  
one R<sup>3</sup> is -H, and the other R<sup>3</sup> is either -H or -CH<sub>3</sub>; and  
each n is 1.

13. (Withdrawn) The method of claim 11, wherein said compound has the chemical structure:

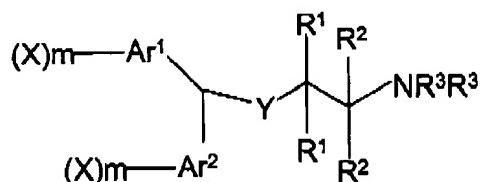


wherein X<sup>1</sup> is either -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, -OCF<sub>3</sub>, -O-alkyl, or -O-acyl;  
X<sup>2</sup> is either -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, -OCF<sub>3</sub>, -O-alkyl, or -O-acyl; and  
R<sup>3</sup> is either -H or -CH<sub>3</sub>;  
or a pharmaceutically acceptable salt thereof.

14. (Withdrawn) The method of claim 13 wherein X<sup>1</sup> is -F, -Cl, -OCF<sub>3</sub> or -CF<sub>3</sub>; and X<sup>2</sup> is either -F, -Cl, -OCH<sub>3</sub>, -CH<sub>3</sub>, -OCF<sub>3</sub> or -CF<sub>3</sub>.

Atty. Dkt. No. 072827-1905

15. (Withdrawn) A method of treating a patient for depression comprising the step of administering to said patient an effective amount of a compound having the chemical structure:



wherein each X is independently selected from the group consisting of -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, —OCF<sub>3</sub>,

-O-alkyl, and -O-acyl; preferably, each X is independently either -F, -Cl, -OCF<sub>3</sub> or -CF<sub>3</sub>;

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently selected from the group consisting of phenyl, naphthyl, thifuranyl, tetrahydronaphthyl, furanyl, tetrahydrofuranyl, pyridyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, cyclohexyl, cycloheptyl, and cyclopentyl; preferably Ar<sup>1</sup> and Ar<sup>2</sup> are independently naphthyl or phenyl; more preferably at least one of Ar<sup>1</sup> and Ar<sup>2</sup> is phenyl; and more preferably, both Ar<sup>1</sup> and Ar<sup>2</sup> are phenyl;

Y is either —CH<sub>2</sub>—, —O—, or —S—;

each R<sup>1</sup> is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl; preferably, each R<sup>1</sup> is -H;

each R<sup>2</sup> is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R<sup>2</sup>'s together are imino; preferably each R<sup>2</sup> is -H;

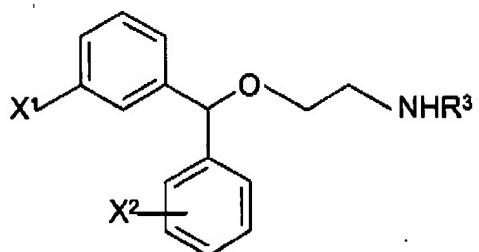
each R<sup>3</sup> is independently selected from the group consisting of -H, alkyl, 2-hydroxyethyl, and alkylphenyl; preferably, each R<sup>3</sup> is independently either -H or -CH<sub>3</sub>; more preferably one R<sup>3</sup> is

-H, and the other R<sup>3</sup> is either -H or -CH<sub>3</sub>; and

each m is independently an integer from 0 to 5; and preferably, each m is independently 0 or 1.

16. (Withdrawn) The method of claim 15, wherein said compound has the chemical structure; Structure VIII

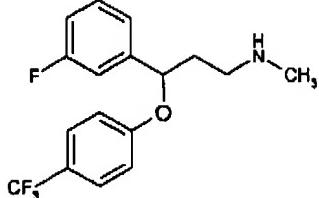
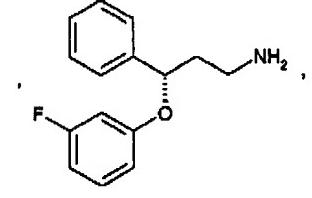
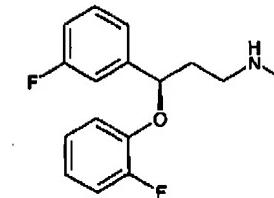
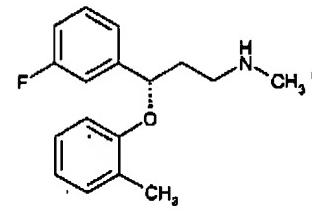
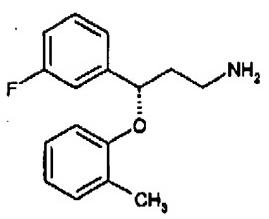
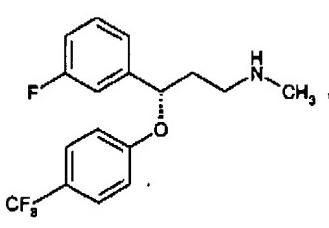
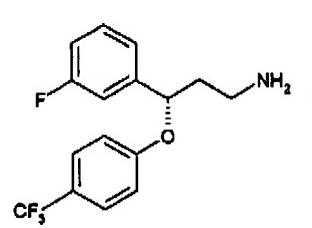
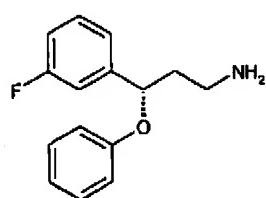
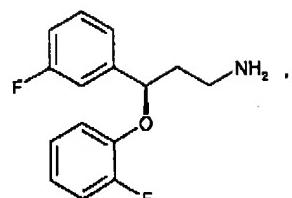
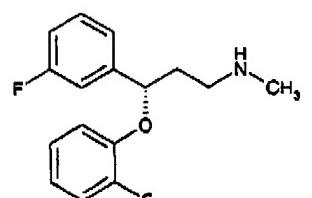
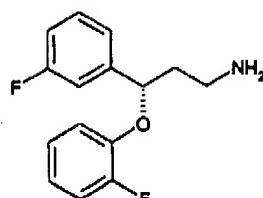
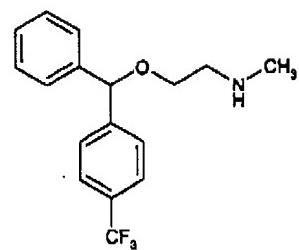
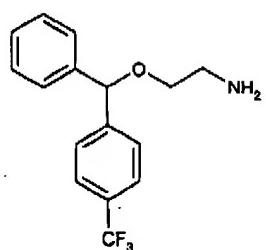
Atty. Dkt. No. 072827-1905



wherein  $X^1$  is independently selected from the group consisting of -H, -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, —OCF<sub>3</sub>, -O-alkyl, or -O-acyl; preferably,  $X^1$  is either -F, -Cl, -OCF<sub>3</sub> and -CF<sub>3</sub>;  $X^2$  is either -Br, -Cl, -F, -I, -CF<sub>3</sub>, alkyl, -OH, —OCF<sub>3</sub>, -O-alkyl, or -O-acyl; preferably,  $X^2$  is independently either -F, -Cl, -OCH<sub>3</sub>, -CH<sub>3</sub>, -OCF<sub>3</sub> or -CF<sub>3</sub>; more preferably,  $X^2$  is either 2-OCH<sub>3</sub>, 2-CH<sub>3</sub>, 3-F, 3-CF<sub>3</sub>, or 4-CF<sub>3</sub>; and R<sup>3</sup> is either -H or CH<sub>3</sub>; or a pharmaceutically acceptable salt thereof.

17. (Withdrawn) A compound having the chemical structure;

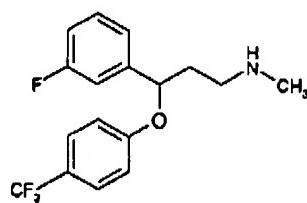
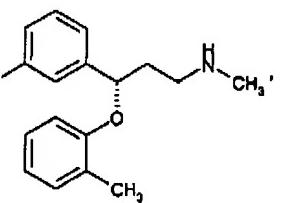
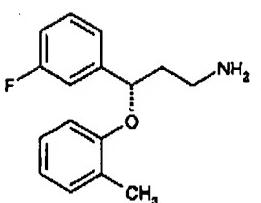
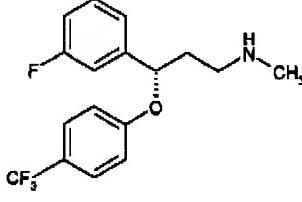
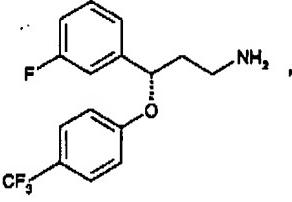
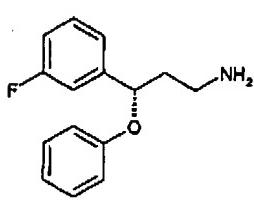
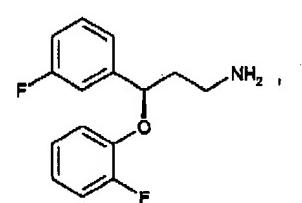
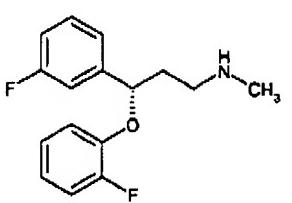
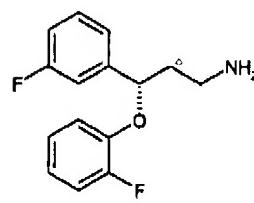
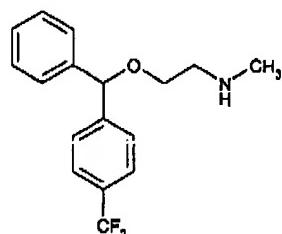
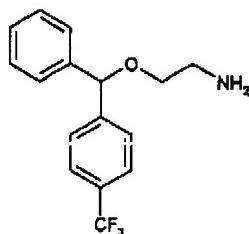
Atty. Dkt. No. 072827-1905



or a pharmaceutically acceptable salt thereof.

Atty. Dkt. No. 072827-1905

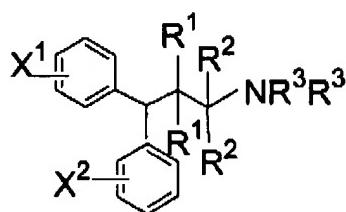
18. (Withdrawn) A method of treating a patient for depression comprising the step of administering to said patient an effective amount of a compound having the chemical structure:



Atty. Dkt. No. 072827-1905

or a pharmaceutically acceptable salt thereof.

19. (Previously presented) The method of claim 3 wherein said compound has the chemical structure:



wherein

X¹ is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, —OCF₃, -O-alkyl, or -O-acyl;

X² is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, —OCF₃, -O-alkyl, or -O-acyl;

each R¹ is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl;

each R² is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R²'s together are imino

each R³ is independently selected from the group consisting of -H, alkyl, 2-hydroxyethyl, and alkylphenyl;

or a pharmaceutically acceptable salt thereof.

20. (Previously presented) The method of claim 19, wherein

each X is independently either -F, -Cl, -OCF₃ or -CF₃;

each R¹ is -H;

each R² is -H; and

one R³ is -H, and the other R³ is either -H or -CH₃.

Atty. Dkt. No. 072827-1905

21. (New) The method of claim 5, wherein  $X^1$  and  $X^2$  are F, and  $R^3$  is -H.
21. (New) The method of claim 21, wherein  $X^2$  is at the 3-position.
23. (New) The method of claim 5, wherein  $X^1$  and  $X^2$  are F, and  $R^3$  is -CH<sub>3</sub>.
24. (New) The method of claim 23, wherein  $X^2$  is at the 3-position.